

cyclohexypeptide-1

of commercial gateways or other similar uses is prohibited and may result in loss of user privileges and other penalties.

* * * * * STN Columbus * * * * *

FILE 'HOME' ENTERED AT 14:07:02 ON 11 JUN 2004

=> file medline caplus biosis embase scisearch agricola		
COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'MEDLINE' ENTERED AT 14:07:30 ON 11 JUN 2004

FILE 'CAPLUS' ENTERED AT 14:07:30 ON 11 JUN 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'BIOSIS' ENTERED AT 14:07:30 ON 11 JUN 2004
COPYRIGHT (C) 2004 BIOLOGICAL ABSTRACTS INC.(R)

FILE 'EMBASE' ENTERED AT 14:07:30 ON 11 JUN 2004
COPYRIGHT (C) 2004 Elsevier Inc. All rights reserved.

FILE 'SCISEARCH' ENTERED AT 14:07:30 ON 11 JUN 2004
COPYRIGHT 2004 THOMSON ISI

FILE 'AGRICOLA' ENTERED AT 14:07:30 ON 11 JUN 2004

=> s cyclic (p) hexapeptide
L1 2429 CYCLIC (P) HEXAPEPTIDE

=> s cyclohexapeptid?
L2 432 CYCLOHEXAPEPTID?

=> s l1 or l2
L3 2707 L1 OR L2

=> s propanolamine
L4 9770 PROPANOLAMINE

=> s l3 (p) l4
L5 5 L3 (P) L4

=> duplicate remove l5
DUPLICATE PREFERENCE IS 'CAPLUS, BIOSIS'
KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):n
PROCESSING COMPLETED FOR L5
L6 4 DUPLICATE REMOVE L5 (1 DUPLICATE REMOVED)

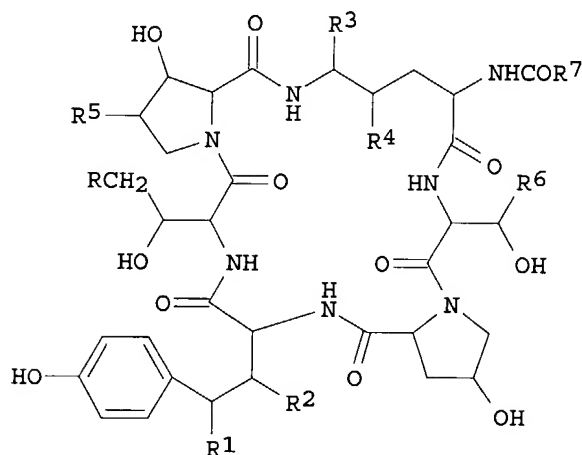
=> d l6 1-4 ibib abs

L6 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 1
ACCESSION NUMBER: 1999:518280 CAPLUS
DOCUMENT NUMBER: 131:144854
TITLE: Preparation of **cyclohexapeptidyl**
propanolamine compounds as antibiotics
INVENTOR(S): Hammond, Milton L.; Zambias, Robert A.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: U.S., 29 pp., Cont.-in-part of U.S. Ser. No. 771,017,
abandoned.
CODEN: USXXAM

cyclohexapeptide-1

DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5939384	A	19990817	US 1992-936561	19920903
CA 2079171	AA	19930402	CA 1992-2079171	19920925
CA 2079171	C	20001003		
EP 535959	A1	19930407	EP 1992-308974	19921001
EP 535959	B1	19970115		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
JP 06234795	A2	19940823	JP 1992-263719	19921001
JP 07121958	B4	19951225		
AT 147757	E	19970215	AT 1992-308974	19921001
ES 2098455	T3	19970501	ES 1992-308974	19921001
PRIORITY APPLN. INFO.:			US 1991-771017	B2 19911001
			US 1992-936561	A 19920903
OTHER SOURCE(S):			MARPAT 131:144854	
GI				



I

AB Title compds. I [R = CH₂NR₈R₉, CH₂N+R₈R₉R₁₀ Z⁻; R₁, R₂, R₄ = independently H, OH; R₃ = H, OH, C₁-4 alkoxy, PhCH₂O; R₅ = H; R₆ = H, Me; R₇ = C₉-21 alkyl, C₉-21 alkenyl, C₁-10 alkoxyphenyl, C₁-10 alkoxyphenyl; R₈, R₉ = independently H, C₁-4 alkyl, CH₂Ph; R₁₀ = C₁-4 alkyl; R₈R₉ = (CH₂)₄₋₆; Z⁻ = anion of a pharmaceutically acceptable salt] and pharmaceutically acceptable salts and compns. were prepared as extremely active antibiotics. Thus, dehydration of 2.08 g carboxamide I [R = CONH₂, R₁ = R₂ = R₃ = R₄ = OH, R₅ = H, R₆ = Me, R₇ = (CH₂)₈CHMeCH₂CHMeEt] with 550 mg. cyanuric chloride in DMF in the presence of 4Å. mol. sieves gave 880 mg nitrile I (R = CN, R₁-7 = same). Reduction of 210 mg nitrile I (R = CN) with 151 mg NaBH₄, and 104 mg CoCl₂·6H₂O in 6 mL MeOH gave 110 mg I (R = CH₂NH₂) (II) as an AcOH addition salt after chromatog. II showed activity against a variety of Candida and Cryptococcus organisms. It was also 99% effective in reducing Pneumocystis carinii cysts in rats when dosed at 0.300 mg/kg.

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 4 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
 ACCESSION NUMBER: 1999:521532 BIOSIS
 DOCUMENT NUMBER: PREV199900521532
 TITLE: Cyclohexapeptidyl propanolamine

cyclohexypeptide-1

compounds.
 AUTHOR(S): Balkovec, James M. [Inventor, Reprint author]; Hammond, Milton L. [Inventor]; Zambias, Robert A. [Inventor]
 CORPORATE SOURCE: North Plainfield, NJ, USA
 ASSIGNEE: Merck and Co., Inc.
 PATENT INFORMATION: US 5948753 Sep. 07, 1999
 SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Sep. 7, 1999) Vol. 1226, No. 1. print.
 CODEN: OGUPE7. ISSN: 0098-1133.
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 ENTRY DATE: Entered STN: 3 Dec 1999
 Last Updated on STN: 3 Dec 1999

L6 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1995:340888 CAPLUS

DOCUMENT NUMBER: 122:299077

TITLE: Preparation and pharmaceutical compositions of
cyclohexapeptidyl propanolamine
 compounds for antibiotics

INVENTOR(S): Balkovec, James M.; Hammond, Milton L.; Zambias, Robert A.

PATENT ASSIGNEE(S): Merck and Co., Inc., USA

SOURCE: PCT Int. Appl., 53 pp.
 CODEN: PIXXD2

DOCUMENT TYPE: Patent

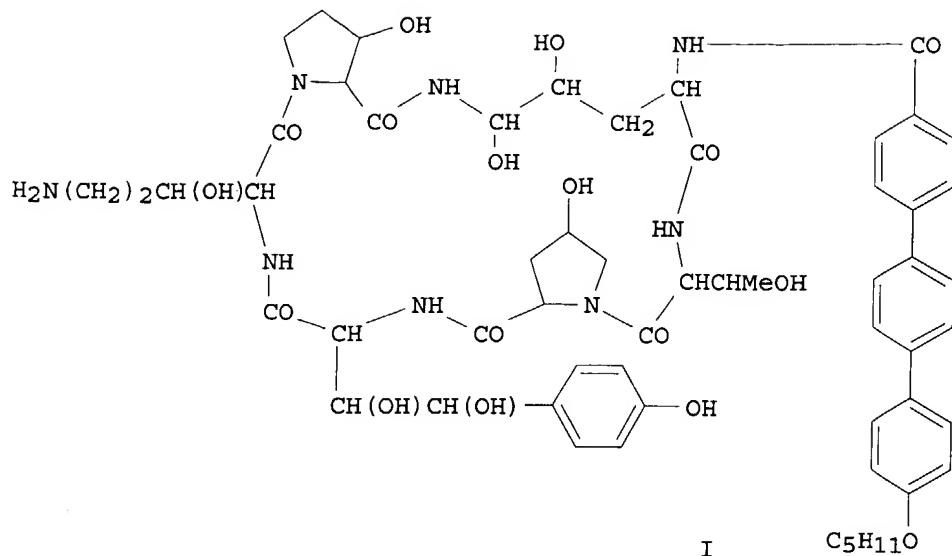
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9425050	A1	19941110	WO 1994-US4169	19940415
W: AU, BB, BG, BR, BY, CA, CN, CZ, FI, HU, JP, KR, KZ, LK, LV, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SI, SK, TT, UA, US, UZ				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5948753	A	19990907	US 1993-58657	19930504
CA 2161150	AA	19941110	CA 1994-2161150	19940415
AU 9469033	A1	19941121	AU 1994-69033	19940415
AU 670384	B2	19960711		
EP 701447	A1	19960320	EP 1994-917261	19940415
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
JP 08509728	T2	19961015	JP 1994-524337	19940415
PRIORITY APPLN. INFO.:			US 1993-58657	A 19930504
			WO 1994-US4169	W 19940415
OTHER SOURCE(S):		MARPAT 122:299077		
GI				

cyclohexypeptide-1



AB **Propanolamine** compds. having a **cyclohexapeptidyl** nucleus (Markush included) and possessing antibiotic activity with phys. properties suitable for direct use in therapeutic compns. are disclosed. A novel process for their preparation is also described. Four such compds. ,e.g. I, are specifically claimed. Tablet, capsule, aerosol, and injection formulations are presented. The compds. of the invention are especially useful for treatment of mycotic infections and are also useful for prevention and treatment of *Pneumocystis carinii* pneumonia.

L6 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1993:581245 CAPLUS

DOCUMENT NUMBER: 119:181245

TITLE: Preparation of **cyclohexapeptidyl**
propanolamine compounds as antibiotics
INVENTOR(S): Hammond, Milton L.; Zambias, Robert A.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: Eur. Pat. Appl., 37 pp.
CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

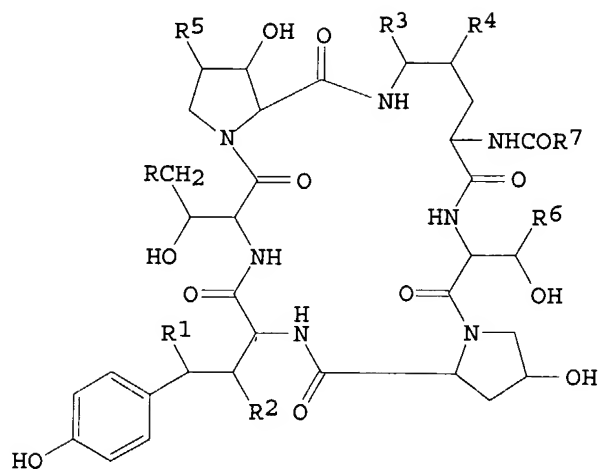
FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 535959	A1	19930407	EP 1992-308974	19921001
EP 535959	B1	19970115		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
US 5939384	A	19990817	US 1992-936561	19920903
PRIORITY APPLN. INFO.:			US 1991-771017	A 19911001
			US 1992-936561	A 19920903
OTHER SOURCE(S):			MARPAT 119:181245	

GI

cyclohexypeptide-1



AB Title compds. I [R = CH₂NR₈R₉, CH₂N+R₈R₉R₁₀ Z⁻; R₁, R₂, R₄ = independently H, OH; R₃ = H, OH, C₁-C₄ alkoxy, PhCH₂O; R₅ = H, OH, Me; R₆ = H, Me; R₇ = C₉-C₁₁ alkyl, C₉-C₂₁ alkenyl, C₁-C₁₀ alkoxyphenyl, C₁-C₁₀ alkoxyphenyl; R₈, R₉, R₁₀ = independently H, C₁-C₄ alkyl, CH₂Ph; R₉R₁₀ = (CH₂)₄, (CH₂)₅; Z⁻ = anion of a pharmaceutically acceptable salt] and pharmaceutically acceptable salts and compns. were prepared as extremely active antibiotics. Thus, dehydration of 2.08 g carboxamide I [R = CONH₂, R₁ = R₂ = R₃ = R₄ = OH, R₅ = H, R₆ = Me, R₇ = (CH₂)₈CHMeCH₂CHMeEt] with 550 mg. cyanuric chloride in DMF in the presence of 4Å mol. sieves gave 880 mg nitrile I (R = CN, R₁-7 = same). Reduction of 210 mg nitrile I (R = CN) with 151 mg NaBH₄, and 104 mg CoCl₂·6H₂O in 6 mL MeOH gave 110 mg I (R = CH₂NH₂) (II) as an AcOH addition salt after chromatog. II showed activity against a variety of Candida and Cryptococcus organisms.

=> d his

(FILE 'HOME' ENTERED AT 14:07:02 ON 11 JUN 2004)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT 14:07:30 ON 11 JUN 2004

```
L1      2429 S CYCLIC (P) HEXAPEPTIDE
L2      432 S CYCLOHEXAPEPTID?
L3      2707 S L1 OR L2
L4      9770 S PROPANOLAMINE
L5      5 S L3 (P) L4
L6      4 DUPLICATE REMOVE L5 (1 DUPLICATE REMOVED)
```

=> s infectious disease

```
L7      123610 INFECTIOUS DISEASE
```

=> s antimicrobial or antifungal or microorganism

```
L8      3149723 ANTIMICROBIAL OR ANTIFUNGAL OR MICROORGANISM
```

=> s l3 (p) l7 (p) l8

```
L9      0 L3 (P) L7 (P) L8
```

=> s l3 (p) (l7 or l8)

```
L10     101 L3 (P) (L7 OR L8)
```

=> s l10 (p) l4

```
L11     1 L10 (P) L4
```

cyclohexypeptide-1

=> s l11 not l6
L12 0 L11 NOT L6

=> s kit or article or package
L13 5348646 KIT OR ARTICLE OR PACKAGE

=> s l13 (p) l3
L14 8 L13 (P) L3

=> duplicate remove l14
DUPLICATE PREFERENCE IS 'MEDLINE, CAPLUS, EMBASE, SCISEARCH'
KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):n
PROCESSING COMPLETED FOR L14
L15 5 DUPLICATE REMOVE L14 (3 DUPLICATES REMOVED)

=> s l15 (p) l4
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L104 (P) L24'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L108 (P) L26'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L110 (P) L27'
L16 0 L15 (P) L4

=> d l15 1-5 ibib abs

L15 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 1
ACCESSION NUMBER: 2004:317682 CAPLUS
TITLE: Synthesis of azine-type heterocyclic compounds and
their conversion into functional molecules
AUTHOR(S): Katoh, Akira; Saito, Ryota
CORPORATE SOURCE: Dep. of Engineering, Seikei University, Musashino-shi,
Tokyo, 180-8633, Japan
SOURCE: Yuki Gosei Kagaku Kyokaishi (2004), 62(4), 335-346
CODEN: YGKKAE; ISSN: 0037-9980
PUBLISHER: Yuki Gosei Kagaku Kyokai
DOCUMENT TYPE: Journal
LANGUAGE: Japanese

AB We have focused on the synthesis of azine-type heterocyclic compds. and
their conversion into useful functional mols. In this **article**,
the following points were reviewed. 1) 6-Amino-2, 3-
dimorpholinoquinoxalines bearing the amino acid residues at C-6 position
were found to be highly-sensitive fluorescent chiral derivatization
reagents. 2) A new tripodal heterocyclic hexadentate ligand, in which
three sets of 3-hydroxy-4(1H)-pyridinone and ethyleneoxy chain are linked
to tris(carboxyethoxymethyl)ethane was synthesized. The allosteric
binding of alkali metal ions to a pseudocryptand formed by the ligand and
Ga(III) was discussed. 3) Hydroxyazine-type linear and **cyclic**
hexapeptides were newly synthesized. The iron(II) complex-forming
tendency, the absolute configuration, the stability constant, the iron(II)
removal from human transferrin, and the growth-promotion activity were
discussed. 4) Oxovanadium complexes of 3-hydroxy-4(1H)-pyridinones were
synthesized. The spectroscopic characterization of the complexes was
carried out on the basis of ¹H-, ⁵¹V-NMR, IR, UV-VIS, FAB MS, ESI MS and
ESR spectra, and **cyclic** voltammetry (CV). Further, an extremely
high insulin-mimetic activity of bis(1,4-dihydro-2-methyl-1-phenyl-4-
thioxo-3-pyridinolato)zinc(II) complex was also discussed.

L15 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:28430 CAPLUS
TITLE: Conformational properties of cyclic peptides
containing 2-aminocycloalkane carboxylic acids

cyclohexypeptide-1

AUTHOR(S): Strijowski, U.; Sewald, N.
CORPORATE SOURCE: Department of Chemistry, University of Bielefeld,
Bielefeld, D-33501, Germany
SOURCE: Peptides 2002, Proceedings of the European Peptide
Symposium, 27th, Sorrento, Italy, Aug. 31-Sept. 6,
2002 (2002), 288-289. Editor(s): Benedetti, Ettore;
Pedone, Carlo. Edizioni Ziino: Castellammare di
Stabia, Italy.
CODEN: 69EYXG; ISBN: 88-900948-1-8
DOCUMENT TYPE: Conference
LANGUAGE: English

AB A number of 2-aminocycloalkane carboxylic acids (ACAC) were synthesized and
were used as mimics for proline in a series of **cyclic** penta- and
hexapeptides containing parts of a binding epitope of VCAM-1.
Peptides were synthesized with Fmoc/tBu/trityl protection on 2-chloro
trityl resin with TBTU/DIPEA on an Advanced ChemTech 496 MOS. The
synthesized peptides have the sequence c-(Ser-ACAC-Leu-Asp-Asn-) and
c-(Ser-ACAC-Leu-Asp-Ile-Asn-) with different proline mimetics. The
interproton distances have been used as restraints for mol. modeling using
the GROMACS **package**.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 3 OF 5 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 1999203772 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10101224
TITLE: 2-pyridylthioureas: novel nonpeptide somatostatin agonists
with SST4 selectivity.
AUTHOR: Liu S; Crider A M; Tang C; Ho B; Ankersen M; Stidsen C E
CORPORATE SOURCE: Division of Basic Pharmaceutical Sciences, School of
Pharmacy, Northeast Louisiana University, Monroe, LA
71209-0470, USA.
SOURCE: Current pharmaceutical design, (1999 Apr) 5 (4) 255-63.
Ref: 59
Journal code: 9602487. ISSN: 1381-6128.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199906
ENTRY DATE: Entered STN: 19990618
Last Updated on STN: 19990618
Entered Medline: 19990608

AB Somatostatin [somatotropin release-inhibiting factor (SRIF)] is a
cyclic tetradecapeptide that is a potent inhibitor of growth
hormone (GH) secretion from the anterior pituitary. In addition to the
inhibitory effects on GH-release, SRIF-14 and SRIF-28, a 28-amino acid
form of SRIF extended from the N-terminal end, inhibit the release of a
variety of other peptides including glucagon, insulin, and gastrin, and
both peptides act as neurotransmitters and neuromodulators in the central
nervous system and the periphery. SRIF exerts its potent inhibitory
effects following binding to high affinity SRIF receptors (sst1-5) that have
been identified on target tissues. The recent cloning of five ssts has
confirmed that the effects of SRIF are mediated by a family of G
protein-coupled receptors (sst1-5). Based on structural and
pharmacological properties sst2, sst3, and sst5 belong to the SRIF1
receptor subclass, and the sst1 and sst4 subtypes comprise the SRIF2
subclass. The major difference between these two subclasses is that SRIF1
receptors bind octapeptide and **hexapeptide** SRIF-14 analogs with
high affinity, while SRIF2 receptors bind these analogs with drastically
reduced affinity. A screening program was initiated to identify a lead

cyclohexypeptide-1

nonpeptide with affinity for sst1-5 receptors. The search focused on a scaffold with the following attachments: (1) a heteroaromatic nucleus to mimic the Trp8 residue, (2) a nonheteroaromatic nucleus to mimic Phe7, and (3) a primary amine or other basic group to mimic the Lys9 residue of SRIF-14. Using these criteria, a novel thiourea (NNC 26-9100, 17) was discovered as a structural lead. The key fragments in this compound are a heteroaromatic moiety (pyridine), an aromatic group, and a basic imidazole group connected through a thiourea scaffold. Compound 17 exhibited a $K_i = 6$ nM at sst4 receptors with a 100-fold sst4/sst2 selectivity and was shown to be a full agonist at this receptor subtype. This **article** will review the literature on the design and development of nonpeptide somatostatin receptor ligands and the therapeutic potential of these agents. Furthermore, our work on the development of 2-pyridylthioureas as sst4 receptor agonists will be described.

L15 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1998:637325 CAPLUS

DOCUMENT NUMBER: 130:34771

TITLE: Mimicking extended conformations of protease substrates: designing cyclic peptidomimetics to inhibit HIV-1 protease

AUTHOR(S): Reid, Robert C.; Fairlie, David P.

CORPORATE SOURCE: Centre for Drug Design and Development, University of Queensland, Brisbane, Australia

SOURCE: Advances in Amino Acid Mimetics and Peptidomimetics (1997), 1, 77-107

CODEN: AAAMF9

PUBLISHER: JAI Press Inc.

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review with 55 refs. There are many examples of structurally distinct **cyclic** peptides that potently regulate biol. processes (e.g. Curr. Med. Chemical 1995, 2, 654-686), but the method of altering their structures to obtain optimal bioactivity is still largely trial and error and thus is painstakingly slow. In this **article** we describe a more rational approach to inhibitor design that focuses on directly mimicking the conformations of peptidic substrate analogs that bind to the protease of Human Immunodeficiency Virus type 1 (HIVPR). This application of inhibitor design to the specific example of HIVPR is illustrative of a general approach to the structural mimicry of receptor-binding conformations of substrates for other proteases. The macrocycles are easily synthesized, conformationally rigid, proteolytically stable, water and lipid soluble, and can be readily varied by altering the size or substituents of a cycle. Such mols. promise to be important mechanistic probes of biol. processes and potential drug leads. A novel hypothesis that extended (strand) substrate conformations are selectively recognized by proteolytic enzymes in general is demonstrated here for HIV-1 protease and supported by our evidence elsewhere for this and other proteases. Evidence includes (1) a consensus extended conformation in X-ray crystal structures of all substrate-mimicking peptidic inhibitors bound to HIV-1 protease, (2) slower processing for turn- or helix-favoring peptide substrates, (3) lack of turn/helical/sheet structure in peptide and also protein substrates that are most rapidly degraded by HIV-1 protease, and (4) factors that promote stretching of the amide bond for substrate processing. Based upon this apparent conformational selection by HIV-1 protease of peptides and analogs in extended strand conformations, we have designed macrocycles that constrain segments of peptide sequences to an extended conformation. These include **cyclic** replacements for N-terminal tri- and tetra-peptides, C-terminal tri- and tetra-peptides, and bicyclic **hexapeptide** analogs which replace both ends. X-ray crystal structures show that these are all structural mimics of protease-binding conformations of substrate analogs. Mol. modeling and NMR spectroscopic studies identify the extent of conformational

cyclohexypeptide-1

restriction afforded by the macrocycles. This structural mimicry leads to functional mimicry, since the **cyclic** compds. selectively inhibit HIV-1 protease at nanomolar concns. when attached to appropriate peptidic and non-peptidic appendages. Unlike acyclic peptide analogs which do not inhibit HIV-1 replication in cells, these macrocycles are pre-organized for receptor-binding, less conformationally flexible than acyclic components of peptidomimetic inhibitors, more resistant to proteolysis than their acyclic analogs, and lipophilic enough to penetrate cell membranes for antiviral activity. This regioselective fixing of the conformation of components of inhibitors for HIV-1 protease may also be useful in designing structural and functional peptidomimetics for substrates of other proteolytic enzymes. The design, synthesis, structure and activities of inhibitors of HIV-1 protease are now described, focusing on some of our work toward incorporating cycles into peptidomimetics.

REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 5 OF 5 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN

ACCESSION NUMBER: 95234621 EMBASE

DOCUMENT NUMBER: 1995234621

TITLE: Echinocandin lipopeptide antifungal agents: New agents and recent chemical modification studies.

AUTHOR: Debono M.

CORPORATE SOURCE: Eli Lilly and Company Inc., Lilly Corporate Center, Indianapolis, IN 46285, United States

SOURCE: Expert Opinion on Therapeutic Patents, (1995) 5/8 (771-786).

ISSN: 1354-3776 CODEN: EOTPEG

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; General Review

FILE SEGMENT: 004 Microbiology
037 Drug Literature Index

LANGUAGE: English

SUMMARY LANGUAGE: English

AB The search for new and effective antifungal agents has been intensified by the increase in the incidence of opportunistic infections due to immunological diseases and aggressive immunosuppressive chemotherapy. Natural products have provided several novel leads in this field. Of these the echinocandin lipopeptides are of special interest due to their fungicidal properties and low toxicity. Their mode of action uniquely targets fungal cell wall biosynthesis by inhibiting the production of β -(1,3)-D-glucan, an essential cell wall component. Echinocandin B (ECB) consists of a **cyclic hexapeptide** whose N-terminus is acylated with linoleic acid. Other natural products of this class have closely related structures with some modification of the **cyclic** peptide and/or the N-acyl fatty acid chain. Although these natural products share excellent antifungal activity, especially against *Candida albicans*, and low toxicity, further improvements in therapeutic and solubility properties were sought through chemical modification. Major efforts have been ongoing at both Merck and Lilly in the quest for natural and semisynthetic echinocandin lipopeptides which will provide novel clinical candidates with a unique mode of action. This **article** describes the development of this class of compounds by reviewing both the primary and patent literature.

=> d his

(FILE 'HOME' ENTERED AT 14:07:02 ON 11 JUN 2004)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT 14:07:30 ON 11 JUN 2004

cyclohexypeptide-1

```
L1          2429 S CYCLIC (P) HEXAPEPTIDE
L2          432 S CYCLOHEXAPEPTID?
L3          2707 S L1 OR L2
L4          9770 S PROPANOLAMINE
L5           5 S L3 (P) L4
L6           4 DUPLICATE REMOVE L5 (1 DUPLICATE REMOVED)
L7         123610 S INFECTIOUS DISEASE
L8         3149723 S ANTIMICROBIAL OR ANTIFUNGAL OR MICROORGANISM
L9           0 S L3 (P) L7 (P) L8
L10          101 S L3 (P) (L7 OR L8)
L11           1 S L10 (P) L4
L12           0 S L11 NOT L6
L13         5348646 S KIT OR ARTICLE OR PACKAGE
L14           8 S L13 (P) L3
L15           5 DUPLICATE REMOVE L14 (3 DUPLICATES REMOVED)
L16           0 S L15 (P) L4

=> s toda a?/au
L17          752 TODA A?/AU

=> s matsuya t?/au
L18          580 MATSUYA T?/AU

=> s mizuno h?/au
L19          3570 MIZUNO H?/AU

=> s matsuda h?/au
L20          17535 MATSUDA H?/AU

=> s murano k?/au
L21          477 MURANO K?/AU

=> s barrett d?/au
L22          3082 BARRETT D?/AU

=> s ogino t?/au
L23          3263 OGINO T?/AU

=> s matsuda k?/au
L24          9411 MATSUDA K?/AU

=> s l17 or l18 or l19 or l20 or l21 or l22 or l23 or l24
L25          38544 L17 OR L18 OR L19 OR L20 OR L21 OR L22 OR L23 OR L24

=> s l25 and l3
L26           4 L25 AND L3

=> duplicate remove l26
DUPLICATE PREFERENCE IS 'CAPLUS, BIOSIS'
KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):n
PROCESSING COMPLETED FOR L26
L27           4 DUPLICATE REMOVE L26 (0 DUPLICATES REMOVED)

=> d l27 1-4 ibib abs

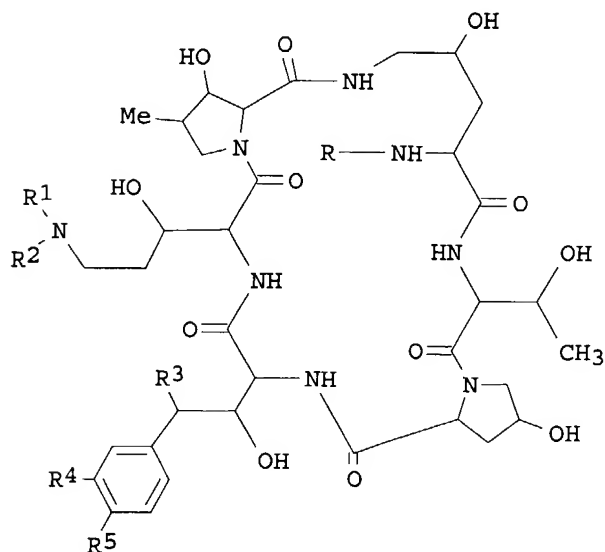
L27  ANSWER 1 OF 4  CAPLUS  COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:      2001:618024  CAPLUS
DOCUMENT NUMBER:       135:180954
TITLE:                 Synthesis of cyclic hexapeptide
                        derivatives for use as antimicrobial or antifungal
                        agents in humans or animals
INVENTOR(S):           Toda, Ayako; Matsuya, Takahiro;
                        Mizuno, Hiroaki; Matsuda, Hiroshi;
```

cyclohexypeptide-1

Murano, Kenji; Barrett, David;
Ogino, Takashi; Matsuda, Keiji
PATENT ASSIGNEE(S): Fujisawa Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 207 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001060846	A1	20010823	WO 2001-JP1204	20010220
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
AU 2001034095	A5	20010827	AU 2001-34095	20010220
EP 1259535	A1	20021127	EP 2001-906140	20010220
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
BR 2001008792	A	20021203	BR 2001-8792	20010220
JP 2003523349	T2	20030805	JP 2001-560230	20010220
RU 2224765	C1	20040227	RU 2002-125463	20010220
NZ 520808	A	20040326	NZ 2001-520808	20010220
US 2003083238	A1	20030501	US 2002-30161	20020130
NO 2002003697	A	20021014	NO 2002-3697	20020806
PRIORITY APPLN. INFO.:			AU 2000-5752	A 20000221
			AU 2000-9552	A 20000821
			AU 2000-2344	A 20001228
			WO 2001-JP1204	W 20010220

OTHER SOURCE(S): MARPAT 135:180954
GI



cyclohexypeptide-1

AB Cyclic polypeptides [(I); R, R1 (independently) = H, acyl; R2 = hydroxyalkyl; R3 = H, OH; R4 = H, OH, alkoxy, HO3SO-; R5 = OH, acyloxy], useful as antimicrobial or antifungal agents, or as β -1,3-glucan synthase inhibitors (no data), for use in prophylactic and/or therapeutic treatment of infectious diseases in humans or animals, were prepared. A variety of substituted acyl R groups were prepared and coupled with the cyclopeptide. Thus, I [R = 4-[2-[4-[4-[5-methoxypentyloxy]piperidin-1-yl]phenyl]imidazo[2,1-b][1,3,4]thiadiazol-6-yl]phenylcarbonyl; R1,R3 = H; R2 = CH(CH2OH)2; R4 = HO3SO; R5 = OH (II)] was prepared in four steps from the starting protected cyclic peptide sodium salt and activated ester of substituted benzoic acid (preparation given). In in vitro tests of antimicrobial activity in mouse serum against *Candida albicans* FP-633, II had MIC <0.3 μ g/mL.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 2 OF 4 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2001:510397 BIOSIS
DOCUMENT NUMBER: PREV200100510397
TITLE: **Cyclic hexapeptides** with antimicrobial activity.
AUTHOR(S): Ohki, Hidenori [Inventor, Reprint author]; **Murano, Kenji** [Inventor]; Tojo, Takashi [Inventor]; Shiraishi, Nobuyuki [Inventor]; **Matsuya, Takahiro** [Inventor]; **Matsuda, Hiroshi** [Inventor]; **Mizuno, Hiroaki** [Inventor]; **Barrett, David** [Inventor]; **Matsuda, Keiji** [Inventor]; Kawabata, Kohji [Inventor]
CORPORATE SOURCE: Takarazuka, Japan
ASSIGNEE: Fujisawa Pharmaceutical Co., Ltd., Osaka, Japan
PATENT INFORMATION: US 6232290 May 15, 2001
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (May 15, 2001) Vol. 1246, No. 3. e-file. CODEN: OGUPE7. ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 31 Oct 2001
Last Updated on STN: 23 Feb 2002

AB This invention relates to new polypeptide compounds represented by general formula (I), wherein R1, R2, R3 and R4 are as defined in the description or a salt thereof which has antimicrobial activities (especially, antifungal activities), inhibitory activity on beta-1,3-glucan synthase, to process for preparation thereof, to a pharmaceutical composition comprising the same, and to a method for prophylactic and/or therapeutic treatment of infectious diseases including *Pneumocystis carinii* infection (e.g. *Pneumocystis carinii* pneumonia) in a human being or an animal.
##STR1##

L27 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:772658 CAPLUS
DOCUMENT NUMBER: 133:335462
TITLE: Preparation of **cyclic hexapeptides** having antibiotic activity
INVENTOR(S): Tojo, Takashi; Ohki, Hidenori; Shiraishi, Nobuyuki; **Matsuya, Takahiro**; **Matsuda, Hiroshi**; **Murano, Kenji**; **Barrett, David**; **Ogino, Takashi**; **Matsuda, Keiji**; Ichihara, Masaharu; Hashimoto, Norio; Kanda, Atsushi; Ohigashi, Atsushi
PATENT ASSIGNEE(S): Fujisawa Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 449 pp. CODEN: PIXXD2
DOCUMENT TYPE: Patent

cyclohexypeptide-1

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000064927	A1	20001102	WO 2000-JP2710	20000425
W: JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 1173472	A1	20020123	EP 2000-917469	20000425
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2003501347	T2	20030114	JP 2000-614276	20000425
PRIORITY APPLN. INFO.:				
			AU 1999-9997	A 19990427
			WO 2000-JP2710	W 20000425
OTHER SOURCE(S): MARPAT 133:335462				
GI				

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB **Cyclic hexapeptides** I [R1 = H, acyl; R2, R3 = H, cyano, (un)substituted alkyl, acyl, heterocyclyl, alkylidenyl; R4 = H, OH; R5 = H, OH, alkoxy, hydroxysulfonyloxy; R6 = OH, acyloxy] or their salts were prepared for use as antimicrobials, especially fungicides. Thus, **cyclic peptide II** [R1 = p-[5-[4'-(2-methoxyethoxy)[1,1'-biphenyl]-4-yl]thiazol-2-yl]benzoyl], prepared via N-acylation reaction, showed MIC <0.3 µg/mL for inhibition of *Candida albicans*.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:511176 CAPLUS

DOCUMENT NUMBER: 131:144853

TITLE: **Cyclic hexapeptides** having antimicrobial activity

INVENTOR(S): Ohki, Hidenori; Murano, Kenji; Tojo, Takashi; Shiraishi, Nobuyuki; Matsuya, Takahiro; Matsuda, Hiroshi; Mizuno, Hiroaki; Barrett, David; Matsuda, Keiji; Kawabata, Kohji

PATENT ASSIGNEE(S): Fujisawa Pharmaceutical Co., Ltd., Japan; et al.

SOURCE: PCT Int. Appl., 470 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9940108	A1	19990812	WO 1999-JP538	19990205
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				

cyclohexypeptide-1

CA 2320416	AA	19990812	CA 1999-2320416	19990205
AU 9922998	A1	19990823	AU 1999-22998	19990205
AU 756792	B2	20030123		
BR 9907967	A	20001017	BR 1999-7967	19990205
EP 1053247	A1	20001122	EP 1999-902855	19990205
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
TR 200003064	T2	20010221	TR 2000-200003064	19990205
JP 2001522377	T2	20011113	JP 1999-540287	19990205
RU 2219185	C2	20031220	RU 2000-123404	19990205
ZA 9900985	A	19990810	ZA 1999-985	19990208
US 6232290	B1	20010515	US 1999-446101	19991222
NO 2000003996	A	20001009	NO 2000-3996	20000808
JP 2004067699	A2	20040304	JP 2003-322336	20030912
PRIORITY APPLN. INFO.:			AU 1998-1728	A 19980209
			AU 1998-3138	A 19980423
			JP 1999-540287	A3 19990205
			WO 1999-JP538	W 19990205
OTHER SOURCE(S):			MARPAT 131:144853	
GI				

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Polypeptides I [R1 = H, (un)substituted arylaminoalkanoyl, aroyl, arylalkanoyl, or alkanoyl, amino protective group, heptylnaphthoyl, hexylnaphthoyl; R2 = H, OH; R3 = OH, hydroxysulfonyloxy, alkoxy; R4 = OH, alkoxy] or their salts were prepared as antimicrobial activities (especially, antifungal activities). Thus, cyclic peptide II, prepared via N-acylation using 4-[5-[4-(6-methoxyhexyloxy)phenyl]-1,3,4-thiadiazol-2-yl]benzoic acid benzotriazol-1-yl ester, showed MIC 0.0625 µg/mL for inhibition of *Candida albicans*.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d his

(FILE 'HOME' ENTERED AT 14:07:02 ON 11 JUN 2004)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT 14:07:30 ON 11 JUN 2004

L1	2429 S CYCLIC (P) HEXAPEPTIDE
L2	432 S CYCLOHEXAPEPTID?
L3	2707 S L1 OR L2
L4	9770 S PROPANOLAMINE
L5	5 S L3 (P) L4
L6	4 DUPLICATE REMOVE L5 (1 DUPLICATE REMOVED)
L7	123610 S INFECTIOUS DISEASE
L8	3149723 S ANTIMICROBIAL OR ANTIFUNGAL OR MICROORGANISM
L9	0 S L3 (P) L7 (P) L8
L10	101 S L3 (P) (L7 OR L8)
L11	1 S L10 (P) L4
L12	0 S L11 NOT L6
L13	5348646 S KIT OR ARTICLE OR PACKAGE
L14	8 S L13 (P) L3
L15	5 DUPLICATE REMOVE L14 (3 DUPLICATES REMOVED)
L16	0 S L15 (P) L4
L17	752 S TODA A?/AU
L18	580 S MATSUYA T?/AU
L19	3570 S MIZUNO H?/AU
L20	17535 S MATSUDA H?/AU

cyclohexypeptide-1

L21 477 S MURANO K?/AU
L22 3082 S BARRETT D?/AU
L23 3263 S OGINO T?/AU
L24 9411 S MATSUDA K?/AU
L25 38544 S L17 OR L18 OR L19 OR L20 OR L21 OR L22 OR L23 OR L24
L26 4 S L25 AND L3
L27 4 DUPLICATE REMOVE L26 (0 DUPLICATES REMOVED)

=> log y

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

78.84

79.05

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE

TOTAL

ENTRY

SESSION

CA SUBSCRIBER PRICE

-6.24

-6.24

STN INTERNATIONAL LOGOFF AT 14:17:02 ON 11 JUN 2004

	Type	L #	Hits	Search Text	DBs	Time Stamp	Comments	Error Definition	Errors
1	BRS	L1	541	cyclic same hexapeptide	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/06/11 13:43			0
2	BRS	L2	121	cyclohexapeptide\$2	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/06/11 13:43			0
3	BRS	L3	647	1 or 2	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/06/11 13:43			0
4	BRS	L4	3057	propanolamine	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/06/11 13:44			0
5	BRS	L5	10	3 same 4	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/06/11 13:53			0
6	BRS	L6	26192	infectious adj disease	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/06/11 13:53			0
7	BRS	L7	212601	microorganism or antimicrobial or antifungal	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/06/11 13:54			0
8	BRS	L8	65	3 same (6 or 7)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/06/11 13:55			0
9	BRS	L9	0	8 same 4	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/06/11 13:55			0
10	BRS	L10	0	5 same (6 or 7)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/06/11 13:55			0
11	BRS	L11	127271 8	kit or package or article	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/06/11 13:57			0
12	BRS	L12	0	5 same 11	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/06/11 13:57			0
13	BRS	L14	3	toda adj ayako.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/06/11 13:58			0
14	BRS	L15	5	matsuya adj takahiro.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/06/11 13:58			0
15	BRS	L16	154	mizuno adj hiroaki.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/06/11 13:59			0
16	BRS	L17	1614	matsuda adj hiroshi.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/06/11 13:59			0

	Type	L #	Hits	Search Text	DBs	Time Stamp	Comments	Error Definition	Error Count
17	BRS	L18	16	murano adj kenji.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/06/11 14:00			0
18	BRS	L19	134	barrett adj david.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/06/11 14:00			0
19	BRS	L20	188	ogino adj takashi.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/06/11 14:01			0
20	BRS	L21	109	matsuda adj keiji.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/06/11 14:01			0
21	BRS	L22	2185	14 or 15 or 16 or 17 or 18 or 19 or 20 or 21	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/06/11 14:02			0
22	BRS	L23	2	22 and 3	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/06/11 14:02			0

=> d his

(FILE 'HOME' ENTERED AT 14:07:02 ON 11 JUN 2004)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA'
ENTERED AT
14:07:30 ON 11 JUN 2004

L1 2429 S CYCLIC (P) HEXAPEPTIDE
L2 432 S CYCLOHEXAPEPTID?
L3 2707 S L1 OR L2
L4 9770 S PROPANOLAMINE
L5 5 S L3 (P) L4
L6 4 DUPLICATE REMOVE L5 (1 DUPLICATE REMOVED)
L7 123610 S INFECTIOUS DISEASE
L8 3149723 S ANTIMICROBIAL OR ANTIFUNGAL OR MICROORGANISM
L9 0 S L3 (P) L7 (P) L8
L10 101 S L3 (P) (L7 OR L8)
L11 1 S L10 (P) L4
L12 0 S L11 NOT L6
L13 5348646 S KIT OR ARTICLE OR PACKAGE
L14 8 S L13 (P) L3
L15 5 DUPLICATE REMOVE L14 (3 DUPLICATES REMOVED)
L16 0 S L15 (P) L4
L17 752 S TODA A?/AU
L18 580 S MATSUYA T?/AU
L19 3570 S MIZUNO H?/AU
L20 17535 S MATSUDA H?/AU
L21 477 S MURANO K?/AU
L22 3082 S BARRETT D?/AU
L23 3263 S OGINO T?/AU
L24 9411 S MATSUDA K?/AU
L25 38544 S L17 OR L18 OR L19 OR L20 OR L21 OR L22 OR L23 OR L24
L26 4 S L25 AND L3
L27 4 DUPLICATE REMOVE L26 (0 DUPLICATES REMOVED)

=> log y